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Oncogenic Virus Studies in Nonhuman Primates under the Special Virus Cancer Program

R. F. KINARD and H. RABIN

Viral Leukemia and Lymphoma Branch, National Cancer Institute, National Institutes of Health, Bethesda, Md. and Department of Virology and Cell Biology, Litton Bionetics, Inc., Kensington, Md.

In 1962, the National Cancer Institute (NCI) initiated viral oncology programs in nonhuman primates. The history and composition of this overall program along with a statement of its principal goals have been reviewed recently [3, 4]. Programs for production and inoculation of simians were begun with an aim to induce leukemia of human origin in an experimental primate host and to recover the causative virus, establish laboratory strains of it, confirm its pathogenicity for humans through seroepidemiological studies, and develop an effective control measure for the disease. These goals basically remain unchanged. The program was originally conceived by Dr. G. ZUBROD and Dr. W. R. BRYAN. In 1964, the Special Virus Leukemia Program (SVLP) directed by Dr. F. J. RAUSCHER, assumed responsibility for the primate studies. In 1968, the SVLP was broadened to include other neoplasms and was renamed the Special Virus Cancer Program (SVCP). The SVCP, currently headed by Dr. J. B. MOLONEY, continues its support of primate production and inoculation programs.

As this is a rather dynamic program its projects have varied extensively since its inception. The purpose of this report is to present the composition of the current program. In doing so, we will discuss the project, the principal primate species used, the major viruses under study, and the general work scope. We are including in the discussion only those projects in which breeding colonies are an essential part of the individual program.

The Litton Bionetics, Inc. Program, Kensington, Md.

This contractor has an established breeding and inoculation program of macaques, mainly *Macaca mulatta* but also including *M. fascicularis* and

M. radiata. These animals are all hand reared and are maintained in isolators when under study. Current production of rhesus monkeys is set at 225 new-borns per year. Attempts are being made to establish similar although somewhat smaller colonies of several New World species, principally *Saguinus fuscicollis*, *Aotus trivirgatus*, *Saimiri sciureus*, and *Cebus albifrons*. Adults of these New World species, obtained commercially, are currently available for study. A small colony of the prosimian species *Galago crassicaudatus* is located at this facility, along with small numbers of inoculated individuals of several other species being held for observation. The work scope and viruses under study include: investigations of the natural history and possible oncogenicity of the Mason-Pfizer monkey virus, an agent associated with a breast tumor of a rhesus monkey [1]; studies of oncogenicity and immunology of *Herpesvirus saimiri*, a herpesvirus of squirrel monkey origin [7]; attempts to infect and transform rhesus monkey cells *in vitro* and produce tumors in rhesus monkeys with RD-114 virus, an agent associated with a human rhabdomyosarcoma [5]; and attempts to transmit lymphosarcoma in rhesus monkeys from material originating from spontaneously-occurring rhesus monkey lymphosarcomas [8]. In addition to these programs, inoculations with other selected virus and tumor materials are also performed. The program at Litton Bionetics, Inc. is presently under the direction of Dr. D. A. VALERIO and Dr. H. RABIN.

The Rush-Presbyterian-St. Luke's Medical Center Program, Chicago, Ill.

This program is under the direction of Drs. L. G. WOLFE and F. DEINHARDT. The principal species bred are *S. fuscicollis* and *S. nigricollis*. Other species in use include *S. oedipus* and *Saimiri sciureus*. The number of new-born marmosets produced per year is greater than 100. The program consists of studies concerning bioassay, antigenicity, oncogenicity, and enzymology of simian sarcoma virus type 1 and simian sarcoma associated virus type 1 [9, 10]; attempted oncogenesis with RD-114 virus; and studies on the natural history and oncogenicity of HVS and of the characterization of HVS-infected lymphoid cell lines. Other studies include investigations of feline sarcoma virus and the Epstein-Barr virus.

The Lincoln Park Zoo Program, Chicago, Ill.

This program is solely concerned with the breeding of marmosets (*S. fuscicollis* and *S. nigricollis*) under the direction of Dr. L. FISHER. There

are approximately 107 adult monkeys in this colony, and the over 100 viable young produced per year are used either as breeding stock or are made available for experimental programs within the SVCP but principally for the Rush-Presbyterian-St. Luke's Medical Center Program.

*The Southwest Foundation for Research and Education Program,
San Antonio, Tex.*

A program for the breeding of chimpanzees, *Pan troglodytes*, is supported with Dr. S. S. KALTER as director. The goal of this program is to provide the SVCP with newborn chimpanzees with two of three newborn animals designated for experimental study as determined by the NCI. A total of 15 animals is presently in the colony, including two breeding age males, six breeding age females, one juvenile male, two juvenile females, three infant males, and one infant female. Approximately five newborn chimpanzees are produced annually.

*The Yerkes Regional Primate Research Center, Emory University
Program, Atlanta, Ga.*

This program is directed toward documenting and characterizing tumors which arise in a colony of irradiated and/or aging rhesus monkeys and in breeding selected animals of this group to evaluate possible genetic damage and occurrence of neoplasia in their progeny. At present, the colony includes 65 adult monkeys ranging in age from 13 to 19 years, of which 48 were exposed to various radiation regimens in 1956-1958. 16 are nonirradiated, and one was added to the study due to the presence of an abdominal adenocarcinoma. There are also eight offspring ranging in age up to four years. Of the total number of deaths in this colony, 33 % were related to tumors. Of the last four monkeys which died, three had malignant neoplasms. At present, three animals in the colony have tumors including an adenocarcinoma, a seminoma, and an uncharacterized tumor adjacent to the ileum. Specimens from the tumors and from the monkeys bearing them are made available for study within the SVCP. The program is directed by Dr. H. M. McCCLURE.

*New England Regional Primate Research Center, Harvard University
Program, Southboro, Mass.*

A program is being initiated with Dr. L. V. MELENDEZ as director. The

work scope will involve investigations of herpes-type viruses isolated from various species of New World monkeys. Principally, investigations will be made of the biological characterization and of the pathogenesis for several species of New World and Old World primates of *Herpesvirus ateles*, a recently-described virus of black spider monkey (*Ateles geoffroyi*) origin [6], and of the effectiveness of attenuated HVS in preventing disease inducible by parent virus. Additionally, several other herpes-type virus isolates will be investigated for oncogenic and oncolytic properties in nonhuman primates. The primate species under study will include five New World species: *A. trivirgatus*, *S. oedipus*, *C. albifrons*, *Ateles* sp., and *Saimiri sciureus*; and three Old World species: *M. mulatta*, *M. fascicularis*, and *Cercopithecus aethiops*.

*The Comparative Oncology Laboratory, University of California,
Davis Program, Davis, Calif.*

A program for the study of simian sarcoma virus type 1 and an oncornavirus associated with spontaneous gibbon lymphosarcoma [2] is directed by Drs. L. K. BUSTAD and T. G. KAWAKAMI. Investigations of these viruses are in areas of biological and physicochemical characterization, pathogenicity, and immunology. The laboratory maintains a small breeding colony of marmosets (*S. fuscicollis* and *S. oedipus*) and is attempting to establish a breeding colony of gibbons (*Hylobates lar*).

Former Programs

The breeding program to produce and inoculate newborn baboons (*Papio anubis* and *P. cynocephalus*) operated by Baylor College of Medicine, Houston, Tex. and the Southwest Foundation for Research and Education under the direction of Dr. J. L. MELNICK has been discontinued. However, a number of baboons previously inoculated at Baylor are still being maintained under observation.

The program at the Institute for Comparative Biology of the Zoological Society of San Diego, San Diego, Calif. has also been terminated. This program emphasized breeding of small species of primates (adult about 1 kg body weight or less) and had been successful in breeding several species of primates including *Cercopithecus (Miopithecus) talapoin*, *Cercopithecus*

pygerythrus, *Saimiri sciureus*, *Callithrix jacchus*, *Saguinus mystax* and *Galago crassicaudatus*. Tumor virus studies performed on this program included those with Rous sarcoma virus, feline sarcoma virus, simian sarcoma virus type 1, and HVS. Dr. R. COOPER, formerly director of this program, is currently serving with the Peace Corps in Colombia, South America where he is participating in population studies of squirrel monkeys.

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Authors' addresses: ROY KINARD, DVM, Viral Leukemia and Lymphoma Branch, National Cancer Institute, National Institutes of Health, *Bethesda, MD 20014*; HARVEY RABIN, PhD, Director, Department of Virology and Cell Biology, Litton Bionetics, Inc., 5510 Nicholson Lane, *Kesington, MD 20795 (USA)*